

**REMARKS**

This Amendment, filed in reply to the Office Action dated September 2, 2009, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-5 and 7-10 are rejected. Claim 6 is objected to. Claim 1 is amended herewith to incorporate the subject matter of Claim 3 therein, and to improve clarity and conciseness. Claims 2 and 4 are amended herewith solely to improve clarity. Claim 3 is canceled herewith without prejudice or disclaimer. Claims 15, 17 and 19 have been amended to correct claim dependency. New Claim 21 is introduced. Support for the subject matter of Claim 21 can be found throughout the specification as originally filed, and at, for example, page 8, lines 29-33.

No new matter is added by way of this Amendment. Entry and consideration of this Amendment are respectfully requested.

**Withdrawn Rejections**

1. Applicants thank the Examiner for withdrawal of the rejection of Claim 6 under 35 U.S.C. § 112, first paragraph.
2. Applicants thank the Examiner for withdrawal of all rejections of record under 35 U.S.C. § 103(a).

**Claim 7 is Enabled Under 35 U.S.C. § 112, First Paragraph**

On page 2 of the Office Action, Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

In making the rejection, the Examiner appears to take the position that, in the absence of a specific deposit of a mutant of *B. subtilis* SD142, and the requisite assurances (*i.e.*, a Statement of Availability), it would require undue experimentation to practice the invention as claimed in Claim 7.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants note that, through withdrawal of the rejection of Claim 6 under 35 U.S.C. § 112, first paragraph, the Office acknowledges that the specification is enabling to practice Applicants' invention using *B. subtilis* SD142. However, the rejection posits that, to practice Applicants' invention using a mutant of *B. subtilis* SD142 without embarking on undue experimentation, a deposit of a mutant of *B. subtilis* SD142, and a Statement of Availability pertaining thereto, is required. Applicants strongly disagree.

Relevant law holds that a deposit is necessary when one of skill in the art would be unable to practice an invention as claimed without undue experimentation in the absence of access to a deposit. Applicants, however, have deposited the *B. subtilis* SD142 strain, and provided a Statement of Availability pertaining thereto, thus enabling one of skill in the art to practice the claimed method with this strain. Logically then, enablement of the subject matter of Claim 7 would only require deposit of a *B. subtilis* SD142 mutant if it would require undue experimentation for one of skill in the art in possession of *B. subtilis* SD142 to produce a mutant thereof. However, such is not the case.

Applicants respectfully point out that the *B. subtilis* SD142 deposit, and submitted Statement of Availability pertaining thereto, also serves to enable the subject matter of Claim 7; for example, one of skill in the art could apply any of the plethora of routine mutagenesis

techniques known in the art at the time of the invention (*e.g.* transposon mutagenesis, UV irradiation) to *B. subtilis* SD142, without embarking on undue experimentation, to produce a mutant strain of *B. subtilis* SD142 that retains production of iturin A and its homologues. Indeed, Applicants respectfully point out that the instant specification provides extensive experimental guidance to allow one of skill in the art to *produce* such mutants, and describes facile screening assays to allow one of skill in the art to efficiently screen and *identify* mutants of *B. subtilis* SD142 possessing equivalent, increased, or reduced, iturin A production vis-à-vis *B. subtilis* SD142. Specifically, the specification describes methods for the production of mutants through chemical mutagenesis, and physical mutagenesis (such as UV- and gamma-irradiation). The specification also discloses that iturin A production by such mutants can be rapidly and effectively determined by culturing these mutants on TBAB media containing sheep blood, and assessing the zone of clearing following such culture. See paragraphs [0068]-[0073] of the specification as published.

In view of the detailed guidance set forth in the specification, coupled with the knowledge in the art at the time of the invention, Applicants respectfully submit that any experimentation required to practice the full scope of Claim 7 would not have been undue, but rather, would have been routine, requiring no more than the application of routine methods and techniques for bacterial mutagenesis and screening, both of which are set forth in the specification, and were well-known in the art. The test of enablement is whether one reasonably skilled in the art could make or use the invention from disclosures in the patent coupled with information known in the art without undue experimentation. See *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). Further, under the rules of patent law, enablement is not precluded by the necessity for experimentation. Indeed, it is well-settled that the test of

enablement is not whether any experimentation is required, but whether, if experimentation is necessary, is it undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Relevant law holds that even extended periods of experimentation may not be undue if those of skill in the art are given sufficient direction or guidance as to how the experimentation should proceed. See *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). The specification clearly provides such.

In view of the foregoing, Applicants respectfully submit that the full scope of Claim 7 is enabled subject matter. Claim 21 is enabled for the same reasons.

Withdrawal of the rejection is respectfully requested.

**Claims 1, 2, 4, 5, 8, 9 and 10 are Patentable Under 35 U.S.C. § 103(a)**

On page 3 of the Office Action, Claims 1-5, 8, 9 and 10 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Phae *et al.*, in view of DeMain *et al.* and Gary *et al.*, each of record, and further in view of Sloma *et al.* (WO 98/22598).

In making the rejection, the Examiner appears to take the position that recitation of “wherein the microbe produces iturin A and its homologues in the medium to a concentration of 1.5 g/L or more” in Claim 1 is merely an intended result of the culturing step recited in the claim, and on this basis, contends that this recitation is not afforded patentable weight. The Examiner cites M.P.E.P. § 2111.04 in support of this contention.

The Examiner relies upon Phae *et al.*, DeMain *et al.* and Gary *et al.* essentially for the same reasons as those of record. However, the Examiner acknowledges that neither Phae *et al.*, DeMain *et al.*, nor Gary *et al.*, discloses using soybean powder in a growth medium. In an attempt to rectify this deficiency, the Examiner relies upon Sloma *et al.*, who allegedly discloses

that *B. subtilis* can be cultured in a liquid medium containing 4% soybean flour, sucrose, and Na<sub>2</sub>HPO<sub>4</sub>, citing page 26, lines 29-31. The Examiner appears to contend that one of ordinary skill in the art would readily have employed soybean flour in the liquid medium of Phae *et al.*, because they would have understood soybean flour as an “art-recognized equivalent” of polypepton.

Regarding the subject matter of examined Claim 3, the Examiner acknowledges Applicants’ Rule 132 Declaration establishing that *B. subtilis* NB22 produces substantial amounts of surfactin, *i.e.*, more than 50 ppm. However, the Examiner contends that, in view of Sloma *et al.*, one of ordinary skill in the art would readily have modified *B. subtilis* NB22 to reduce its surfactin production. Specifically, the Examiner asserts that Phae *et al.* discloses that *B. subtilis* NB22 produces significant amounts of foam, citing page 118, column 1; the Examiner contends that Sloma *et al.* discloses that foam production by *Bacillus* species limits the productivity of fermentation, and protein recovery, citing page 2, lines 14-25. The Examiner further contends that Sloma *et al.* discloses that modifying *Bacillus* species to produce less surfactin creates conditions conducive for the production of polypeptides (by reducing foam production), and that surfactin production can be reduced by 95%, citing page 6, lines 19-21. The Examiner thus contends that one of ordinary skill in the art would readily have modified *B. subtilis* NB22 in the method of Phae *et al.* to decrease foam production, in order to increase iturin A production. The Examiner contends that modifying *B. subtilis* NB22 according to the methods of Sloma *et al.* would result in a strain producing less than 50ppm surfactin, thus rendering obvious the subject matter of Claim 3.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants note that Claim 1 as amended recites that the *Bacillus* microbe is cultured in a liquid medium containing 2% mass or more of soybean powder or defatted soybean powder until iturin A and its homologues are present in the medium at a concentration of 1.5g/L or more. Thus, Claim 1 as amended does not recite “wherein the microbe produces iturin A and its homologues in the medium to a concentration of 1.5 g/L or more,” and as such, M.P.E.P. § 2111.04 is inapplicable. Applicants also note that Claim 1 is amended to incorporate the subject matter of Claim 3 therein.

Turning to the substance of the rejection, the Examiner contends that Sloma *et al.* provides a reason that would have prompted a person of ordinary skill in the relevant field to modify the *B. subtilis* strain of Phae *et al.* to reduce surfactin production, by as much as 95%, so as to enhance iturin A production. Applicants strongly, but respectfully, disagree.

First, Applicants respectfully submit that the rejection fails to proffer a credible reason that would have prompted a person of ordinary skill in the relevant field *at the time of the invention* to modify the *B. subtilis* strain of Phae *et al.* to ablate surfactin production; the law mandates that a reason *that would have prompted a person of ordinary skill in the relevant field* to combine the elements in the way the claimed new invention does must be made explicit. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). Contrary to the Examiner’s position, one of ordinary skill in the relevant field would not have been prompted to modify the *B. subtilis* strain of Phae *et al.* to ablate surfactin production in order to *increase* iturin A expression, because they would instantly recognize that the method of Phae *et al.* is directed to the purification of iturin A by *specific isolation of the foam fraction*, which is enriched in iturin A. See page 118, 1<sup>st</sup> paragraph. Indeed, as shown in Figure 5 of Phae *et al.*, the greater the foam production, the greater the iturin A production. Clearly then, one of

ordinary skill in the relevant field would not have been prompted to modify the method of Phae *et al.* by ablating foam production, because they would appreciate that such would drastically decrease the amount of iturin A recovered by the method of Phae *et al.*

For the same reason, one of ordinary skill in the art would not have possessed any expectation of success in increasing iturin A production in the method of Phae *et al.* by decreasing foaming; rather, because those of ordinary skill in the art were aware that iturin A is a *lipopeptide*, and thus possesses surfactant and foaming properties, they would expect exactly the *opposite, i.e.*, decreased iturin A recovery, by reducing surfactin production.

Moreover, Applicants respectfully submit that one of ordinary skill in the relevant field would not have been prompted to modify the method of Phae *et al.*, in view of Sloma *et al.*, also because they would not readily understand that an increase in polypeptide production by reducing foaming (allegedly disclosed by Sloma *et al.*) also correlates with an increase in iturin A production; this is because they would have understood that iturin A is a lipopeptide, possessing surfactant and foaming properties, and thus that reducing foaming would reduce iturin A recovery. Moreover, as shown in Examples 11 and 12 of Sloma *et al.*, strains having different foaming abilities produced the *same* amounts of protein (*i.e.*, NOVAMYL), further serving to dissuade one of ordinary skill in the art from reducing surfactin production.

Second, and independent of the above, Applicants respectfully submit that the proposed modification of the method of Phae *et al.* posited in the rejection, *i.e.*, to decrease foam production, also renders the method of Phae *et al.* unsatisfactory for its intended purpose. Because the intended purpose of the method of Phae *et al.* is enhanced isolation of iturin A by foam separation (See Abstract and Title), it is clear that ablating foam production in the method of Phae *et al.* would render the method unsatisfactory for its intended purpose. It is settled law

that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Third, as another indicia of the nonobviousness of the present invention, Applicants respectfully point out that Phae *et al.* effectively teaches away from the presently claimed invention, by disclosing the criticality of foam production. It is well-settled law that a reference teaches away when a person of ordinary skill in the art, upon reading it, would be discouraged from following the path set out in the reference, or would be led in a path divergent from the path taken by the inventor. See *Monarch Knitting Mach. Corp v. Sulzer Morat GmbH*, 139 F.3d, 877, 45 USPQ2d 1977 (Fed. Cir. 1998); *Para-Ordnance Mfg. v. SGS Importers Int'l Inc.*, 73 F.3d1085, 37 USPQ2d 1237 (Fed. Cir. 1995); and *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). Clearly, one of ordinary skill in the art reading Phae *et al.* and Sloma *et al.* would be led in a path *divergent* from the presently claimed invention (*i.e.*, employing a *Bacillus* strain which produces 50ppm or less of surfactin in the culture medium); as discussed above, they would instantly recognize that foam production is critical to the efficient iturin A isolation by Phae *et al.*, and thus would not have possessed any reason to ablate foam production by decreasing surfactin production.

In view of the foregoing, Applicants respectfully submit that the present invention is not rendered obvious by the cited references.

Withdrawal of the rejection is respectfully requested.



### **Claim Objections**

1. On page 6 of the Office Action, Claim 6 is objected to as depending from a rejected claim. However, the Examiner asserts that this claim would be allowable if re-written in independent form.

Applicants respectfully submit that, in view of the amendments and arguments herein, Claim 1 is allowable subject matter. As such, the objection is moot.

2. On page 6 of the Office Action, Claim 2 is objected to for recitation of “homologs.” The Examiner requests that such be amended to “homologues,” consistent with the remaining claims.

Solely in the interest of advancing prosecution, and without acquiescing to the merits of the objection, Applicants herewith amend Claim 2 to replace recitation of “homologs” with “homologues.” Applicants respectfully submit that the amendment overcomes the objection.

Withdrawal of the objections is respectfully requested.

### **Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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